

We claim:

1. A method for detecting cyclin dependent kinase 5 (Cdk5) activity in a biological sample, which method comprises determining whether Disabled 1 protein (Dab1) in said sample is phosphorylated on a candidate sequence preferred by cdk 5 activity, wherein phosphorylation of Dab1 on said candidate sequence indicates the presence of active Cdk5 in said sample.
2. The method of claim 1 wherein the candidate sequence contains the Cdk5 amino acids consisting of serine 491 and 515.
3. The method of claim 1 wherein the candidate sequence is selected from the group consisting of tryptic peptides QSSPSK (SEQ ID NO:1) and SSASHVSDPTADDIFEEGFESPSK (SEQ ID NO:2).
4. The method of claim 1 wherein said biological sample is derived from an organism selected from the group consisting of mouse and human.
5. The method of claim 1 wherein said biological sample is derived from the group consisting of brain and blood.
6. The method of claim 1 wherein said biological sample is derived from a cell culture.
7. The method of claim 1 wherein said Dab1 phosphorylation occurs *in vivo*.
8. The method of claim 1 which comprises immunoprecipitating said Dab1 from said biological sample prior to said determining step using an antibody that binds to phosphorylated and unphosphorylated Dab1.
9. The method of claim 1 which comprises immunoprecipitating said Dab1 from said biological sample prior to said determining step using an antibody that binds to Dab1 only when it is phosphorylated on a Cdk5 candidate sequence.
10. The method of claim 1 wherein Dab1 phosphorylation is determined using an antibody that binds to Dab1 only when it is phosphorylated on a candidate sequence preferred by Cdk5 activity.

11. The method of claim 10 wherein said antibody is raised against the polypeptide fragment TPAPRQSS(PO<sub>4</sub>)PSKSSA (SEQ ID NO:3 which contains a phosphate group on serine 491).
12. The method of claim 10 wherein said antibody detects Dab1 phosphorylation on amino acids consisting of serine 491 and serine 515.
13. The method of claim 10 wherein said antibody is polyclonal.
14. The method of claim 10 wherein said antibody is monoclonal.
15. The method of claim 10 wherein Dab1 phosphorylation is determined by using techniques consisting of radioimmunoassay, ELISA, "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays, western blots, precipitation reactions, agglutination assays, complement fixation assays, immunofluorescence assays, protein A assays, immunoelectrophoresis assays, mass spectrometry and antibody array.
16. A method for identifying a compound that inhibits or decreases Cdk5 activity which could be used for the treatment of a disease or condition where Cdk5 activity is involved in pathogenesis, which method comprises
- (a) determining whether Dab1 in a test sample is phosphorylated on a candidate sequence preferred by Cdk5 activity in the presence of said compound and active Cdk5 and
- (b) comparing Cdk5 activity in said test sample with Cdk5 activity in a control sample which contains active Cdk5 but lacks the compound, wherein decreased phosphorylation of Dab 1 in said test sample as compared to said control sample indicates a compound that is capable of inhibiting or decreasing Cdk5 activity.
17. The method of claim 16 wherein said condition is selected from the group consisting of Parkinson's disease, Huntington's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), stroke, epilepsy, lissencephaly and trauma.
18. A method for identifying a compound that increases Cdk5 activity which could be used for the treatment of a disease or condition in which Cdk5 activity is involved in pathogenesis, which method comprises

(a) determining whether Dab1 in a test sample is phosphorylated on a candidate sequence preferred by Cdk5 activity in the presence of said compound and active Cdk5 and

(b) comparing Cdk5 activity in said test sample with Cdk5 activity in a control sample which contains active Cdk5 but lacks the compound, wherein increased phosphorylation of Dab1 in said test sample as compared to said control sample indicates a compound that is capable of increasing Cdk5 activity.

19. The method of claim 18 wherein said condition is selected from the group consisting of Parkinson's disease, Huntington's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), stroke, epilepsy, lissencephaly and trauma.

20. A method for treating Alzheimer's disease and ALS comprising administering a therapeutically effective amount of a compound which is identified using the method of claim 16.

21. A method for treating epilepsy and lissencephaly comprising administering a therapeutically effective amount of a compound which is identified using the method of claim 18.

22. A method for detecting neurological disorders in a subject, which method comprises detecting Cdk5 activity in said subject according to the method of claim 1 wherein a decrease of said Dab1 phosphorylation in said biological sample as compared to a control biological sample from a control subject indicates the presence of a neurological disorder.

23. A method for detecting neurological disorders in a subject, which method comprises detecting Cdk5 activity in said subject according to the method of claim 1 wherein an increase of said Dab1 phosphorylation in said biological sample as compared to a control biological sample from a control subject indicates the presence of a neurological disorder.

24. A method for detecting neurological disorders, which method comprises detecting Cdk5 activity according to the method of claim 12 wherein a decrease or lack of said Dab1 phosphorylation in said biological sample as compared to a control

biological sample from a control subject indicates the presence of a neurological disorder.

25. A method for detecting neurological disorders, which method comprises detecting Cdk5 activity according to the method of claim 12 wherein an increase of said Dab1 phosphorylation in said biological sample as compared to a control biological sample indicates the presence of a neurological disorder.

26. A screening kit comprising

(a) an antibody that binds to Dab1 only when it is phosphorylated on a candidate sequence preferred by Cdk5 activity; and

(b) reagents suitable for detecting the binding of said antibody to Dab 1.

27. The screening kit of claim 26 wherein said reagents comprise reagents used in techniques consisting of radioimmunoassay, ELISA, "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays, western blots, precipitation reactions, agglutination assays, complement fixation assays, immunofluorescence assays, protein A assays, immunoelectrophoresis assays, mass spectrometry and antibody array.

28. An antibody that binds to Dab1 only when it is phosphorylated on a candidate sequence preferred by Cdk5 activity.

29. The antibody of claim 28 which is raised against the polypeptide fragment TPAPRQSS(PO<sub>4</sub>)PSKSSA (SEQ ID NO:3 which contains a phosphate group on serine 491).

30. The antibody of claim 28 that detects Dab1 phosphorylation on amino acids consisting of serine 491 and serine 515.

31. A method for quantitating the level of cyclin dependent kinase 5 (Cdk5) activity in a biological sample, which method comprises

(a) determining the amount of Disabled 1 protein (Dab1) in said sample which is phosphorylated on a candidate sequence preferred by Cdk 5 activity, and

(b) determining the total amount of Dab1 in said sample,

wherein the proportion of Dab1 which is is phosphorylated on said candidate sequence represents a quantitative measure of the level of Cdk5 activity in said sample.